

SUPPLEMENTARY MATERIAL

Exhaustion Disorder: A Scoping Review of Research on a Recently Introduced Stress-Related Diagnosis

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| Content | Pages |
|--|--------------|
| Table S1. Full search strategy | 2 |
| Table S2. Overview of excluded but “complementary” studies | 3-6 |
| Tables S3a and S3b. Data-charting of primary publications of quantitative studies investigating exhaustion disorder treatment | 7-10 |
| Table S4. Overview of included empirical studies of individuals diagnosed with exhaustion disorder, ED | 11-17 |
| Table S5. Overview of dissertations | 18-20 |
| References | 21-27 |

Table S1. Full search strategy

| Search Strategy [†] | Medline | Psycinfo | Web of Science |
|------------------------------|--|---|--|
| Interface | Ovid | Ovid | Clarivate Analytics |
| No of hits | 3691 | 2179 | 1804 |
| Field labels | _ exp/ = exploded MeSH term _ / = non exploded MeSH term _ * = truncation of word for alternate endings _ mp. = title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier _ in. = institution | _ exp/ = exploded controlled term _ / = non exploded controlled term _ * = truncation of word for alternate endings _ mp = title, abstract, heading word, table of contents, key concepts, original title, tests measures _ in. = institution | _ TS = topic _ AD = address _ * = truncation of word for alternate endings |
| 1. | exp Stress, Psychological/ | exp Stress/ | TS=burnout |
| 2. | exp Adjustment Disorders/ | exp Adjustment Disorders/ | TS=exhaustion |
| 3. | burnout.mp. | burnout.mp. | TS="psychologic* stress*" |
| 4. | exhaustion.mp. | exhaustion.mp. | TS="occupational stress*" |
| 5. | 1 or 2 or 3 or 4 | 1 or 2 or 3 or 4 | TS="adjustment disorder*" |
| 6. | sweden.mp. or exp Sweden/ | sweden.mp. or exp Sweden/ | 5 OR 4 OR 3 OR 2 OR 1 |
| 7. | (sweden or lund or linkoping or stockholm or gothenburg or umea or uppsala or karlstad or orebro or ostersund or vaxjo).in. | (sweden or lund or linkoping or stockholm or gothenburg or umea or uppsala or karlstad or orebro or ostersund or vaxjo).in. | AD=(sweden OR lund OR linkoping OR stockholm OR gothenburg OR umea OR uppsala OR karlstad OR orebro OR ostersund OR vaxjo) |
| 8. | 6 or 7 | 6 or 7 | 7 AND 6 |
| 9. | 5 and 8 | 5 and 8 | TS=("exhaustion disorder*") |
| 10. | exhaustion disorder*.mp. | exhaustion disorder*.mp. | TS=("exhaustion syndrome*") |
| 11. | exhaustion syndrome*.mp. | exhaustion syndrome*.mp. | TS=("exhaustion depression*") |
| 12. | exhaustion depression*.mp. | exhaustion depression*.mp. | 11 OR 10 OR 9 |
| 13. | 10 or 11 or 12 | 10 or 11 or 12 | 12 OR 8 |
| 14. | 9 or 13 | 9 or 13 | - |

[†]All searches were initially conducted on June 17th 2020 with the aid of librarian Carl Gornitzki, Universitetsbiblioteket, Karolinska Institutet

Table S2. Overview of excluded but “complementary” studies ($N = 39$) with unclear reference to, or self-rated, exhaustion disorder (ED).

| First author | Year | Design | Aim/question |
|--|-------------|-------------------------------|--|
| <i>Lived experience of ED, n = 2</i> | | | |
| Gustafsson ¹ | 2008 | Qualitative | To illuminate the meanings of becoming and being burned out as narrated by healthcare personnel on sick leave because of symptoms of burnout. |
| Håkansson ² | 2010 | Qualitative | To re-analyze the data for its congruence with the Matuska and Christiansen life balance model using a matrix system, and to test the validity of the model. |
| <i>Symptoms, course and context, n = 10</i> | | | |
| Asplund ³ | 2021 | Cross-sectional | To assess the prevalence of self-rated exhaustion disorder (s-ED), describe plausible between-group differences in self-reported health-related factors among employees with or without s-ED, and identify health-related factors associated with s-ED. |
| Broddardottír ⁴ | 2021 | Cross-sectional | To identify ED patients whose fatigue meets criteria for "persistent physical symptoms" (PPS) and explore whether they differ from other ED patients in terms of psychological distress, non-fatigue PPSs and functional impairment, inspecting whether this alternative formulation of the fatigue problem might be more appropriate. |
| Gustafsson ⁵ | 2009 | Cross-sectional, case control | To describe patterns of personality traits among two groups of health-care personnel from the same workplaces, one group on sick leave due to medically assessed burnout, and one group with no indication of burnout, respectively |
| Gustafsson ⁶ | 2010 | Cross-sectional, case control | To elucidate perceptions of conscience, stress of conscience, moral sensitivity, social support and resilience among two groups of health care personnel from the same workplaces, one group on sick leave owing to medically assessed burnout and one group who showed no indications of burnout. |
| Håkansson ⁷ | 2018 | Longitudinal, cohort | To investigate whether perceived occupational imbalance predicts stress-related disorders and possible gender differences. To explore the mediating role of perceived stress in the association between occupational imbalance and stress-related disorders. |
| Höglund ⁸ | 2020 | Cross-sectional | To determine symptom severity of anxiety, depression, insomnia, burnout and somatization in combinations of different age groups and sex. To determine prevalence of caseness of these types of mental ill-health in both absolute and relative terms in the combinations of age groups and sex. |
| Norlund ⁹ | 2011 | Cohort, prospective | To investigate the impact of psychosocial working conditions and coping strategies at work on change in sick leave level for patients on long-term sick leave due to burnout. |

Lindsäter et al 2022; Exhaustion Disorder: Scoping Review of Research

| | | | |
|--|------|---------------------------------|--|
| Stenlund ¹⁰ | 2007 | Case control | To describe gender differences in patients with burnout and compare these patients with a general population with respect to physical, psychosocial and work variables. |
| Söderström ¹¹ | 2012 | Prospective | To identify risk factors for subsequent clinical burnout. |
| Wiegner ¹² | 2015 | Observational, Cohort | To examine to what extent a working age population seeking primary health care perceives stress, as well as symptoms of burnout/exhaustion, depression and anxiety. |
| <hr/> <i>Cognitive functioning, n = 1</i> <hr/> | | | |
| Sandström ¹³ | 2005 | Cross-sectional, case control | To conduct a thorough examination of the cognitive performance of patients with a diagnosis of chronic burnout |
| <hr/> <i>Biological measures, n = 10</i> <hr/> | | | |
| Blix ¹⁴ | 2013 | Cross-sectional, case control | To examine whether chronic work-related stress is associated with changes in brain structure. |
| Bäckström ¹⁵ | 2012 | Cross-sectional, case control | To compare GABA-A receptor sensitivity as indexed by maximal saccadic eye velocity between burnout and control subjects |
| Ekstedt ¹⁶ | 2006 | Repeated measures, case control | To investigate sleep with polysomnography and self-ratings and the diurnal pattern of sleepiness and fatigue in a group suffering from severe occupational burnout. |
| Golkar ¹⁷ | 2014 | Cross-sectional, case control | To investigate whether (1) subjects suffering from occupational stress have an impaired ability to modulate stressful emotions; and whether (2) these subjects show altered amygdala functional connectivity |
| Grossi ¹⁸ | 2005 | Repeated measures, case control | To compare salivary cortisol awakening response between individuals with low, moderate and high burnout scores |
| Heiden ¹⁹ | 2005 | Cross-sectional, case control | To characterize patients with stress-related illnesses by comparing autonomic activity, pressure-pain thresholds, and subjective assessments of health and behavior between patients with stress-related illnesses and control subjects. |
| Jovanovic ²⁰ | 2011 | Repeated measures, case control | To investigate whether enduring daily stress causes widespread limbic dysfunctions, and specific changes of the 5-HT1A receptor. |
| Sandström ²¹ | 2011 | Cross-sectional, case control | To use a multivariate statistical approach to examine whether patients with work-related exhaustion and controls differed on an extensive set of biological, psychological and immunological variables. |
| Sandström ²² | 2012 | Cross-sectional, case control | To compare functional magnetic resonance imaging (fMRI) patterns and diurnal cortisol across three groups: (i) controls, (ii) acute un-medicated patients with unipolar major depression, and (iii) patients on long-term sick leave due to work stress. |
| Savic ²³ | 2015 | Repeated measures, case control | To compare salivary cortisol, cortical thickness, cortical surface area and subcortical volumes between individuals with occupational stress compared to controls. |

| <i>Symptom measurement scales, n = 4</i> | | | |
|--|------|----------------------------|--|
| Glise ²⁴ | 2010 | Longitudinal, cohort | To assess the construct and predictive validity of a new instrument for self-rating of stress-related Exhaustion Disorder (s-ED). |
| Persson ²⁵ | 2016 | Cross-sectional | To benchmark the Lund University Checklist for Incipient Exhaustion (LUCIE) against the s-ED and the Karolinska Exhaustion Disorder Scale, but also against other ED-related concepts such as burnout. |
| Persson ²⁶ | 2017 | Cross-sectional | To examine the relationships of two screening instruments recently developed for assessment of ED with some other well-known inventories intended to assess ED-related concepts and self-reports of job demands, job control, job support, private life stressors, and personality factors. |
| Saboonchi ²⁷ | 2013 | Cross-sectional | To examine the psychometric properties of Karolinska Exhaustion Scale (KES) in its original and revised versions by examining the factorial structure and measures of convergent and discriminant validity. |
| <i>Interventions, n = 12</i> | | | |
| Cerwén ²⁸ | 2016 | Qualitative | To increase understanding of the role of soundscapes in Nature Based Rehabilitation (NBR), |
| Fjellman-Wiklund ²⁹ | 2010 | Qualitative | To explore patients' experiences in a burnout rehabilitation programme with two different rehabilitation groups. |
| Grahn ³⁰ | 2017 | Longitudinal, cohort | To examine return to work a year after the start of participation in nature-based rehabilitation programs with different lengths (8, 12, and 24 weeks). |
| Grossi ³¹ | 2009 | Longitudinal, case control | To determine whether complementary therapy based on a group treatment program could improve the patients' health, physiological markers and work capacity better than the standard individual treatment program offered by the municipal company healthcare. |
| Heiden ³² | 2007 | RCT | To evaluate the effects of a cognitive behavioural training programme and a physical activity programme, compared with usual care, for patients with stress-related illnesses. |
| Nygren ³³ | 2019 | Longitudinal, case control | To examine whether a combination of a multimodal rehabilitation, group-talks with colleagues, and active monitoring (intervention carried out on an all-inclusive hotel in Gran Canaria) leads to improved return-to-work rates in sick-listed teachers with exhaustion disorder compared with treatment as usual. |
| Pálsdóttir ³⁴ | 2014 | Mixed method | To describe and assess changes in participants' experiences of everyday occupations after nature-based vocational rehabilitation and to assess changes regarding symptoms of severe stress and the rate of return to work and possible association with experiencing the occupational value of everyday occupations. |
| Pálsdóttir ³⁵ | 2014 | Qualitative, longitudinal | To explore and illustrate how participants with stress-related mental disorders participating in nature-based rehabilitation experience and describe their rehabilitation process in relation to the role of the natural environments. |

Lindsäter et al 2022; Exhaustion Disorder: Scoping Review of Research

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|------------------------------|------|----------------------------|---|
| Person-Asplund ³⁶ | 2018 | RCT | To evaluate the efficacy of a guided internet-based stress management intervention among distressed managers compared with an attention control group with full access to treatment-as-usual. |
| Sahlin ³⁷ | 2015 | Longitudinal, cohort | To explore the effects of nature-based rehabilitation in patients with exhaustion disorder or stress-related mental disorders. |
| Stenlund ³⁸ | 2009 | RCT | To evaluate effects on psychological variables and sick leave rates by two different group rehabilitation programs for patients on long-term sick leave because of burnout. |
| Stenlund ³⁹ | 2012 | RCT, secondary publication | To evaluate the long-term effects of two different rehabilitation programs for patients on long-term sick leave for burnout. |

RCT, randomized controlled trial

Table S3a. In-depth data-charting of primary publications of quantitative studies included in the review that investigated interventions for exhaustion disorder.

| First author, year | Pre-registration of trial | Design | N | Intervention (n) | Control (n) | Age (mean) | Women (%) | % ED |
|--------------------------------------|---------------------------|--------------------------|-----------------|--|---|-----------------|-----------|------|
| Eskilsson, 2017 ⁴⁰ | No | RCT [†] | 88 | Multimodal rehabilitation (MMR)+ aerobic training (AT) (47) | MMR (41) | 42 | 88 | 100 |
| Finnes, 2017 ⁴¹ | Yes | RCT | 352 | Acceptance and commitment therapy (ACT) (90); Workplace dialogue intervention (WDI) (90); ACT+WDI (90) | Treatment as usual (89) | 46 | 78 | 67 |
| Gerber, 2015 ⁴² | No | Cohort | 169 | MMR+coached exercise (36) | MMR (133) | 43 | 79 | 100 |
| Grensman, 2018 ⁴³ | Retrospective | RCT | 94 | Traditional yoga (TY) (26); Mindfulness-based CBT (MBCBT) (27) | CBT (27) | 44 | 89 | 100 |
| Karlson, 2010 ⁴⁴ | Yes | Prospective case-control | 148 | Convergence dialogue meeting (CDM) (74) | Care as usual (74) | 46 | 78 | 89 |
| Lindegård, 2015 ⁴⁵ | No | Cohort | 69 | MMR (69) | N/A | 43 | 65 | 100 |
| Lindsäter, 2018 ⁴⁶ | Yes | RCT | 100 | Internet-based CBT (ICBT) (50) | Waitlist control (50) | 46 | 85 | 47 |
| Malmberg Gavelin, 2015 ⁴⁷ | No | RCT [†] | 99 | MMR+cognitive training (CT) (53) | MMR (46) | 43 [§] | 85 | 100 |
| Malmberg Gavelin, 2018 ⁴⁸ | Retrospective | RCT [†] | 132 | MMR+CT (44); MMR+AT (47) | MMR (41) | 43 [§] | 84 | 100 |
| Millet, 2009 ⁴⁹ | No | cohort | 32 | Nature/Gardening (32) | N/A | 46 (median) | 100 | 100 |
| Nordh, 2009 ⁵⁰ | No | cohort | 24 [‡] | Forest rehabilitation (24) | N/A | 45 | 57 | 48 |
| Olsson, 2009 ⁵¹ | No | RCT | 60 | Rhodiola rosea (30) | Placebo (30) | 42 [§] | 90 | 100 |
| Ristiniemi, 2014 ⁵² | No | Pre-post, case-control | 44 | African dance (15) | Healthy controls (14); ED controls (15) | 44 [§] | 82 | 100 |
| Salomonsson, 2017 ⁵³ | Yes | RCT | 211 | CBT (64); CBT+Return to work intervention (RWT-I) (80) | RTW-I (67) | 42 | 82 | 59 |
| Sonntag-Öström, 2015 ⁵⁴ | No | RCT | 99 | Forest rehabilitation + MMR (51) | Waitlist + MMR (48) | 45 | 86 | 100 |
| Stenlund, 2009 ⁵⁵ | No | RCT | 82 | Qigong (41) | Basic care (41) | 44 | 83 | 100 |
| van de Leur, 2020 ⁵⁶ | Yes | Cohort | 390 | MMR (390) | N/A | 44 | 88 | 100 |

RCT, randomized controlled trial; CBT, cognitive behavior therapy

Lindsäter et al 2022; Exhaustion Disorder: Scoping Review of Research

[†]Same RCT reporting on different outcomes. Inconsistencies in reported number of participants in the three publications from the same RCT.

[‡]Only baseline data on 21 participants.

[§]Mean age only reported for subgroups. Mean age for total sample calculated by research team (mean across subgroups).

Table S3b. Table S3a continued, illustrating additional data-charting from primary publications of quantitative studies included in the review.

| First author, year | Length of treatment (weeks) | Post-assessment follow-up (months) | Primary outcome(s) | % attrition to post-assessment (Intervention) | % attrition to post-assessment (Control) | ITT † | Selected main finding |
|---------------------------------------|-----------------------------|------------------------------------|--|---|--|-------|---|
| Eskilsson, 2017 ⁴⁰ | 12 MMR + 12 MMR+AT | no | Cognitive test battery | 49 | 22 | no | Episodic memory improved in MMR+AT vs control. No differences on self-reported mental and physical health outcomes. |
| Finnes, 2017 ⁴¹ | 12 | 3, 9 | Net days on sick leave (registry), work ability index | ACT: 27; WDI:42; ACT+WDI: 28 | 27 | yes | No difference in sickness absence (SA) post-assessment. At 9m follow-up, more SA in ACT+WDI compared to TAU. ACT and ACT+WDI improved symptoms more than TAU at post-assessment. |
| Gerber, 2015 ⁴² | 52 | 6, 12 | Self-reported frequency, duration, and intensity of exercise | 0 | 0 | N/A | No differences between coached and general exercise advice. All participants reported increased exercise frequency. |
| Grensman, 2018 ⁴³ | 20 | no | Health-related quality of life (SWED-QUAL) | TY: 19; MBCT: 13 | CBT: 13 | no | All group treatments had equal positive effects on health-related quality of life. |
| Karlson, 2010 ⁴⁴ | unclear | weekly until week 80 | Return-to-work; yes/no (registry) | N/A | N/A | N/A | More participants in the intervention-group had returned to work (89%) after 1,5 years compared to control group (73%). No difference between groups regarding full return to work. |
| Lindegård, 2015 ⁴⁵ | 52 | 6, 12, 18 | Self-reported frequency, duration, and intensity of exercise | 0 | N/A | N/A | Higher compliance with physical activity recommendation was associated with decreased levels of ED symptoms and depression. |
| Lindsäter, 2018 ⁴⁶ | 12 | 6 | Perceived Stress Scale-14 | 2 | 4 | yes | ICBT vs waitlist made large and significant improvements on PSS-14 ($d = 1.09$). |
| Malmberg Gavelin, 2015 ^{47‡} | 12 MMR + 12 MMR+CT | no | Cognitive test battery | 49 | 30 | no | Significant small effects on three of nine transfer tests at post-intervention in MMR+CT vs MMR only. |

Lindsäter et al 2022; Exhaustion Disorder: Scoping Review of Research

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|---------------------------------------|--|-------|--|----------------------------|-----------|-----|--|
| Malmberg Gavelin, 2018 ^{48‡} | 12 MMR + 12 MMR+CT Or 12 MMR+AT | 12 | Global cognitive performance on cognitive test battery | CT:36; AT: 49 | 20 | yes | Higher global cognitive score in the MMR+CT group vs MMR only. No between-group differences in other psychological assessments. |
| Millet, 2009 ⁴⁹ | 21 to 29 | no | Not stated | 0 | N/A | N/A | Reductions in stress and cortisol levels and improvements in sleep and energy post treatment. |
| Nordh, 2009 ^{50‡} | 10 | no | Not stated | N/A | N/A | N/A | Decrease in stress (SCI) and quality of life and an increase in anxiety and depressed mood post-treatment. |
| Olsson, 2009 ⁵¹ | 4 | no | Pines' burnout scale | 3 | 0 | no | Small between-group effects on Pines in favor of the treatment. |
| Ristiniemi, 2014 ⁵² | 4 | no | Nijmegen Symptom Questionnaire | 0 | 0 | N/A | Higher levels of hyperventilation in ED participants vs healthy controls pre-intervention. No between-group effects on hyperventilation at post-intervention assessment. |
| Salomonsson, 2017 ⁵³ | 8-20 CBT; up to 25 CBT+RTW-I; up to 10 RTW-I | 6, 12 | Net days on sick leave (registry); Clinician Severity Rating | CBT: 8; CBT+RTW-I: 6 | RTW-I: 12 | yes | No differences in sick leave. CBT reduced clinician rated symptom severity vs RTW-I at post-intervention. No additional benefit of CBT+RTW-I on symptom reduction. |
| Sonntag-Öström, 2015 ⁵⁴ | 12 forest rehabilitation + 24 MMR | 9 | Not stated | 22 | 4 | no | No significant between-group differences for any of the variables. |
| Stenlund, 2009 ⁵⁵ | 12 | no | Shirom Melamed Burnout Questionnaire-22 | 20 | 15 | yes | No significant between-group differences for any of the variables. |
| van de Leur, 2020 ⁵⁶ | 24 | 12 | Karolinska Exhaustion Disorder Scale; self-rated sick leave | 3 | N/A | N/A | Large symptom reduction post treatment and at follow-up, increased self-reported working time and reduced sick-leave compensation. |

[†]ITT, Intention to treat analysis

[‡]Information about attrition cannot be estimated based on data in the publication.

Table S4. Overview of included empirical studies of individuals diagnosed with exhaustion disorder, ED ($N = 89$)

| First author | Year | Design | Sample size | Women % | Aim of the study |
|--|-------------------|-------------------------------|----------------------|---------|--|
| <i>Lived experience of Exhaustion Disorder (ED), n = 9</i> | | | | | |
| Alsén ⁵⁷ | 2020 | Qualitative | 12 | 58 | Explore ED participants' experience of ED in the early stages of sick leave. |
| Arman ⁵⁸ | 2011 | Qualitative | 18 | 67 | Get a deeper and existential understanding of burnout, by looking at patterns of health, suffering and expressions of understanding of life in a longitudinal perspective. |
| Engebretsen ⁵⁹ | 2018 | Qualitative | 8 | 75 | Assess how the values that go with the biomedical framework affect medical inquiry and the attitudes of the medical profession related to how burnout is understood and treated. |
| Engebretsen ⁶⁰ | 2019 | Qualitative | 8 | 75 | To describe the experience of suffering from burnout while waiting to be recognized as ill, as the diagnosis "Exhaustion disorder" is not recognized in Norway. |
| Engebretsen ⁶¹ | 2020 | Qualitative | 8 | 75 | Explore how ED participants on long-term sick leave deal with the process of coming to terms with their present body in the rehabilitation process. |
| Ericson-Lidman ⁶² | 2007 | Qualitative | 15 | 100 | Describe co-workers' perceptions of signs preceding ED in workmates. |
| Hörberg ⁶³ | 2020 [†] | Qualitative | 12 | 100 | Describe how women with stress-related illness experience well-being in everyday life. |
| Jingrot ⁶⁴ | 2008 | Qualitative | 11 | 73 | Explore the lived experiences of the process leading to ED. |
| Norlund ⁶⁵ | 2013 | Qualitative | 12 | 83 | Explore experiences and thoughts in the process of returning to work in employed individuals with ED. |
| <i>Symptoms, course, and context, n = 13</i> | | | | | |
| Adamsson ⁶⁶ | 2018 | Retrospective medical chart | 115 | 77 | Investigate the frequency of different stress-related complaints present 2 years prior the confirmation of ED diagnosis. |
| Beno ⁶⁷ | 2021 | Cross-sectional | 217 | 74 | To explore whether participants with ED had made any changes in their work situation from the period of treatment and up to 7 years later, as reported at the follow-up. |
| Glise ⁶⁸ | 2012 | Longitudinal, cohort | 228 | 68 | Explore the course of illness (primarily symptoms of burnout) for 18 months among individuals diagnosed and treated for ED and if course of illness was related to sex and age. |
| Glise ⁶⁹ | 2014 | Longitudinal, cohort | 228 | 68 | Explore the prevalence of somatic symptoms in individuals with ED and follow the course of symptoms for 18 months while participating in a multimodal rehabilitation program. |
| Glise ⁷⁰ | 2020 | Longitudinal, cohort | 217 | 74 | To explore perceived recovery, and residual symptoms including fatigue, depression, and anxiety among previous ED patients 7 years after seeking care. |
| Grensman ⁷¹ | 2016 | Cross-sectional, case control | ED 92; Control 88 | 84 | Explore the health-related quality of life (HRQoL), the cause of being ill, and the pharmacological treatment in individuals on sick leave because of ED. |

Lindsäter et al 2022; Exhaustion Disorder: Scoping Review of Research

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|--------------------------|-------------------|----------------------------------|---------------------------------|----|--|
| Grossi ⁷² | 2015 | Cross-sectional | 420 | 77 | Investigate differences in socio-demographic variables, use of medications, quality of sleep and symptoms of anxiety, depression, and fatigue in a sample of Swedish men and women referred to care for ED. |
| Grossi ⁷³ | 2021 | Cross-sectional | 808 | 84 | Assess the prevalence of self-rated hazardous drinking in individuals with ED, and to investigate differences in sociodemographic variables, psychological symptoms, health-related quality of life, and sleep variables between individuals with different drinking patterns. |
| Gulin ⁷⁴ | 2021 | Cross-sectional | 147 | 78 | To investigate whether recovery from ED is associated with obsessive-compulsive personality disorder. |
| Hasselberg ⁷⁵ | 2014 | Mixed method | Part 1: 20 Part 2:100 | 50 | Explore which stressors are reported as important for the onset of illness by individuals seeking medical care for ED, the prevalence of these stressors, and potential gender differences. |
| Maroti ⁷⁶ | 2017 | Cross-sectional, case control | ED 31; CFS 38; Control 30 | 80 | Investigate if there are differences between ED and Chronic fatigue syndrome (CFS) in reaction to self-reported alexithymia and observer-rated emotional awareness. |
| Maroti ⁷⁷ | 2018 | Cross-sectional, case control | ED 31; CFS 38; Control 30 | 80 | Compare quality of life between individuals with ED, CFS, and healthy controls (HC) by using the SF-36 and HADS. |
| Skoglund ⁷⁸ | 2018 [†] | Prospective, medical chart | 192 | 79 | To verify if individuals on antidepressant therapy and on long-term sick leave for mild and moderate depression, anxiety, and stress-related mental disorders have a longer sick leave than individuals treated with psychological and other therapies. |

Cognitive functioning, n = 10

| | | | | | |
|--------------------------|------|---|--|----|---|
| Bartfai ⁷⁹ | 2021 | Cross-sectional | 39 | 90 | To explore the diagnostic potential of the MapCog Spectra and validate the results through simultaneously obtained data on clinical neuropsychological tests. |
| Ellbin ⁸⁰ | 2018 | Cross-sectional, case control | ED 93; Control 111 | 69 | Determine whether a brief test battery such as CAB (cognitive assessment battery) could identify cognitive impairment in individuals seeking healthcare for stress-related exhaustion. |
| Ellbin ⁸¹ | 2021 | Cross-sectional, case control | ED 51; Recovered ED 98; Control 50 | 74 | Investigate self-reported cognitive difficulties, daily life activities, and health/sleep factors in former ED patients who still fulfill the clinical criteria for ED 7–12 years after seeking care. |
| Jonsdottir ⁸² | 2013 | Cross-sectional, case control | ED 33; Control 37 | 77 | To compare cognitive function in individuals with ED and healthy controls and explore if neuropsychological findings were related to severity of illness. |
| Jonsdottir ⁸³ | 2017 | Longitudinal; cross-sectional, case control | ED 30; Control 27 | 60 | Examine if cognitive impairment is still present in patients with ED 2–3 years after seeking care. |
| Krabbe ⁸⁴ | 2017 | Cross-sectional, case control | ED 25; Control 25 | 72 | Explore perceived fatigue and the effects of distraction when performing executive and complex attentional tasks. |

Lindsäter et al 2022; Exhaustion Disorder: Scoping Review of Research

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|---|-------------------|-------------------------------|--|---------------------------|---|
| Nelson ⁸⁵ | 2021 | Cross-sectional, case control | ED 103; Control 58 | 84 | Examine how individuals with ED differ from healthy controls with regard to levels and type of subjective cognitive complaints, and if such complaints are associated with cognitive test performance and psychological distress. |
| Österberg ⁸⁶ | 2009 | Cross-sectional, case control | ED 65; Control 65 | 71 | Explore cognitive problems in ED and the associations between subjective and objective cognitive performance and diurnal cortisol pattern and the DST response. |
| Österberg ⁸⁷ | 2012 | Longitudinal, cohort | 45 | 71 | Determine if recovery from burnout is associated with improved cognitive functioning and if improvement is associated with changes in HPA axis activity and return to work rates. |
| Österberg ⁸⁸ | 2014 | Cross-sectional, case control | Former-ED 54; Control 50 | 73 | Assess long-term cognitive performance after substantial recovery from ED in relation to subjective cognitive complaints and return to active work. |
| <i>Biological measures, n = 24</i> | | | | | |
| Ekstedt ⁸⁹ | 2009 | Longitudinal, case control | ED 23; Control 16 | 72 | Investigate the role of sleep physiology in recovery from burnout/ED and the relation between sleep and changes in fatigue and return to work. |
| Hadrevi ⁹⁰ | 2019 | Cross-sectional, case control | ED 20; Control 21 | 54 | Investigate metabolic functions in individuals diagnosed with ED and to compare them with healthy controls. |
| Jónsdóttir ⁹¹ | 2009 | Cross-sectional, case control | Part 1: ED 42; Control 42 Part 2: ED 89; Control 88 | Part 1: 100 Part 2: 54 | Confirm potential biomarkers of prolonged psychosocial stress in female ED participants suggested in a former study: monocyte chemotactic protein-1 (MCP-1), epidermal growth factor (EGF) and vascular endothelial growth factor (VEGF). |
| Jönsson ⁹² | 2015 | Test-retest, case control | Former ED 14; Pre-ED 17; Control 20 | 51 | Examine whether dysfunctional flexibility of the stress response in the hypothalamus-pituitary-adrenal (HPA) axis and the sympathetic-adreno-medullar (SAM) axes is present during early stages of ED, and still present after recovery. |
| Lennartsson ⁹³ | 2015 | Cross-sectional, case control | ED 17; Control 13 | 37 | Investigate the DHEA-s response during acute psychosocial stress in individuals with ED. |
| Lennartsson ⁹⁴ | 2015 | Cross-sectional, case control | ED 19; Control 37 | 66 | Investigate whether individuals with ED exhibit aberrant cortisol and ACTH responses to acute psychosocial stress compared with healthy individuals. |
| Lennartsson ⁹⁵ | 2015 | Cross-sectional, case control | ED 122; Control 47 | 49 | Investigate DHEA-s levels in individuals with ED compared to healthy controls. |
| Lennartsson ⁹⁶ | 2016 | Longitudinal, cohort | 122 | 49 | Investigate possible changes in DHEA-S levels in ED participants and examine whether these changes are associated with health-development. |
| Lennartsson ⁹⁷ | 2016 [†] | Cross-sectional, case control | ED 54; Non-clinical burnout 52; Control 55 | 60 | To investigate heart rate variability in individuals with ED compared to individuals with non-clinical burnout and to healthy controls. |

Lindsäter et al 2022; Exhaustion Disorder: Scoping Review of Research

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| Lindegård ⁹⁸ | 2019 | Longitudinal, cohort | 88 | 100 | Investigate longitudinal associations between cardiorespiratory fitness and self-reported physical activity levels and the severity of symptoms connected to ED, depression, anxiety, and sleep disturbances among women clinically diagnosed with ED. |
| Malmberg Gavelin ⁹⁹ | 2017 | Cross-sectional, case control; longitudinal | Baseline 55; Follow-up:10; Control 11 | Baseline: 84 Follow-up: 49 | Investigate the association between the key symptom of ED and functional neural response during working-memory processing. Additionally, neural effects of cognitive training (CT) as part of stress rehabilitation were investigated. |
| Malmberg Gavelin ¹⁰⁰ | 2020 | Cross-sectional | 55 | 84 | Investigate cortical and subcortical structural neural correlates of mental fatigue in individuals with ED, and to explore the association between mental fatigue and cognitive functioning. |
| Olsson ¹⁰¹ | 2010 | Cross-sectional, case control | ED 36; Control 19 | 100 | Investigate possible differences between women with stress-related fatigue/ED and healthy women in heart rate variability (HRV) and other autonomic and respiratory measures, task performance and in salivary cortisol response. |
| Savic ¹⁰² | 2018 | Cross-sectional; Longitudinal, case control | ED 48; Control 80; Follow-up: ED 25; Control 19 | Baseline: 59 Follow-up: 61 | Investigate the cerebral effects of chronic occupational stress and its possible reversibility. |
| Savic ¹⁰³ | 2020 | Cross-sectional, case control | ED 30; Control 31 | 51 | Investigate regional glutamate concentrations using single-voxel MR spectroscopy (MRS) in participants with ED. |
| Sjörs ¹⁰⁴ | 2012 | Longitudinal, case control | ED 162; Control 79 | 59 | Investigate differences in HPA axis activity between individuals with ED and healthy controls and to investigate longitudinal changes in HPA axis activity in the ED group during multimodal rehabilitation. |
| Sjörs ¹⁰⁵ | 2013 | Cross-sectional, case control | ED 90; Control 90 | 51 | Test the usability of the allostatic load (AL) index for a clinical population with severe ED. Hypothesis was that AL would be greater in ED sample. |
| Sjörs ¹⁰⁶ | 2015 | Longitudinal, case control | ED 122; Control 98 | 66 | Investigate possible deviations in the diurnal cortisol profiles of individuals with clinically diagnosed ED compared with healthy controls. |
| Sjörs ¹⁰⁷ | 2019 | Cross-sectional, case control | ED 40; Control 40 | 50 | Investigate if circulating levels of EGF, VEGF and BDNF were altered in individuals with ED and if the level of these factors were related to symptom duration and severity in the ED group. |
| Skau ¹⁰⁸ | 2021 | Test-retest, case control | ED 20; Control 20 | 70 | Investigate cognitive performance and functional activity in the PFC during prolonged mental activity in individuals with ED vs healthy controls. |
| Sonntag-Öström ¹⁰⁹ | 2014 | Repeated measures, experimental | 20 | 100 | Investigated differences in perceived restorativeness, mood, attention capacity and physiological reactions when visiting city and forest environments. |
| Wallensten ¹¹⁰ | 2016 | Longitudinal, case control | ED 105; Control 116 | 100 | Examine the role of VEGF, EGF and MCP-1 in women with ED and at least 50% sick-leave and healthy women during a follow-up period of two years. |

Lindsäter et al 2022; Exhaustion Disorder: Scoping Review of Research

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| Wallensten ¹¹¹ | 2021 | Cross-sectional, case control | ED 31; MDD 31; Control 61 | 85 | Examine if astrocyte-derived extracellular vesicles (EV) exist in the peripheral blood of individuals with ED and if concentrations of EVs differ between ED, individuals with major depressive disorder (MDD), and healthy controls. |
| Wallensten ¹¹² | 2021 | Cross-sectional, case control | ED 31; MDD 31; Control 561 | 85 | To compare plasma levels of different isoforms of VEGF, including VEGF121, VEGF165, and VEGF121+VEGF165 (VEGFtotal) in individuals with ED, patients with major depressive disorder (MDD), and healthy controls. |
| Symptom measurement scales, n = 4 | | | | | |
| Axelsson ¹¹³ | 2017 [†] | Longitudinal | 160 | 78 | To study the psychometric properties of the 12-item self-report WHODAS 2.0 when administered online to individuals with anxiety and stress disorders. |
| Beser ¹¹⁴ | 2014 | Cross-sectional, case control | ED 200; Control 117 | 80 | To construct and evaluate a self-rating scale, the Karolinska Exhaustion Disorder Scale (KEDS), for the assessment of ED symptoms. |
| Lundgren-Nilsson ¹¹⁵ | 2012 | Cross-sectional, case control | ED 319; Control 319 | 69 | To examine the properties of the Shirom-Melamed Burnout Questionnaire (SMBQ) for validation of use in a clinical setting. |
| Lundgren-Nilsson ¹¹⁶ | 2013 | Longitudinal | 179 | 70 | To evaluate the Psychological general well-being index (PGWBI) with Rasch- and factor analysis. |
| Interventions, n = 29 | | | | | |
| Adevi ¹¹⁷ | 2012 | Qualitative | 5 | 80 | Explore caregiver perspective on factors considered most essential to the recovery process of patients with ED. |
| Adevi ¹¹⁸ | 2013 | Qualitative | 5 | 80 | Explore the impact of garden therapy on stress-rehabilitation with a special focus on nature. |
| Eskilsson ⁴⁰ | 2017 | RCT [‡] | MMR+AT 47; MMR 41 | 88 | Investigate the effects on cognitive performance and psychological variables of a 12-week aerobic training (AT) program performed at a moderate-vigorous intensity for individuals with exhaustion disorder who participated in a multimodal rehabilitation program (MMR). |
| Eskilsson ¹¹⁹ | 2020 | Qualitative | 13 | 85 | Explore experiences from persons with ED after participating in a 12-week intervention of MMR with either additional computerized cognitive training or aerobic training. |
| Finnes ¹²⁰ | 2017 [†] | RCT | ACT 89; WDI 87; ACT+WDI 88; TAU 88 | 78 | Evaluate the efficacy of 3 interventions targeting sickness absence of workers. Randomization to (a) acceptance and commitment therapy (ACT), (b) a workplace dialogue intervention (WDI), (c) a combination of ACT and WDI, or (d) treatment as usual (TAU). |
| Finnes ¹²¹ | 2017 [†] | RCT, secondary analysis | ACT 89; WDI 87; ACT+WDI 88; TAU 88 | 78 | To evaluate cost-utility of ACT and WDI, both as stand-alone interventions and in combination, compared with treatment as usual (TAU), for employees on sickness absence with mental disorders. |

Lindsäter et al 2022; Exhaustion Disorder: Scoping Review of Research

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| Gerber ⁴² | 2015 | Longitudinal, cohort | Exercise 36; General advice 133 | 79 | Examine the changes in exercise habits during a 12-month MMR treatment and possible differences between general exercise instructions and an additional 18-week coached exercise program. |
| Grensman ⁴³ | 2018 | RCT | TY 32; MBCT 31; CBT 31 | 89 | Assess the effects of a long (20 weeks) treatment with traditional yoga (TY), mindfulness-based cognitive behavioral therapy (MBCT) and cognitive behavioral therapy (CBT; active control) on health-related quality of live (HRQoL) in individuals with ED on sick leave. |
| Karlson ⁴⁴ | 2010 [†] | Longitudinal, case control | CDM 74; Control 74 | 78 | Evaluate the effect of a “convergence dialogue meeting”-intervention (CDM; job-person match through patient-supervisor communication) with individuals being treated for burnout compared to a waitlist control of individuals not wanting the CDM-intervention. |
| Karlson ¹²² | 2014 [†] | Longitudinal, case control | CDM 68; Control 68 | 81 | Whether the effects of CDM-intervention (presented in Karlson, 2010) were sustained or increased further during an additional 12 months, or whether the intervention merely speeded up the course of return to work. |
| Lindegård ⁴⁵ | 2015 | Longitudinal, cohort | 69 | 65 | Investigate whether initially physically inactive individuals diagnosed with ED differ at the 6-month, 12-month and 18-month follow-up regarding burnout (as a primary outcome), depressive symptoms, and anxiety symptoms depending on whether they (mildly or strongly) complied or did not comply with the physical activity recommendations. |
| Lindsäter ¹²³ | 2018 [†] | RCT | ICBT 50; Waitlist 50 | 85 | To investigate the efficacy of internet-delivered cognitive behavioral therapy (ICBT) for individuals suffering from chronic stress, operationalized as adjustment disorder and ED. |
| Lindsäter ¹²⁴ | 2019 [†] | RCT, secondary analysis | ICBT 50; Waitlist 50 | 85 | Evaluate the cost-effectiveness and cost-utility of ICBT for individuals with stress-related disorders in the form of adjustment disorder or ED. |
| Lindsäter ¹²⁵ | 2021 [†] | RCT, secondary analysis | ICBT 50; Waitlist 50 | 85 | To investigate insomnia symptom severity as a putative mediator of treatment response in internet-based CBT for chronic stress, using data from a randomized controlled trial. |
| Malmberg Gavelin ⁴⁷ | 2015 | RCT [‡] | MMR + CT 27; MMR 32 | 85 | Evaluate the effects of Multimodal rehabilitation (MMR) + a cognitive training (CT) intervention in comparison with only MMR on cognitive performance and subjective cognitive complaints. |
| Malmberg Gavelin ⁴⁸ | 2018 | RCT [‡] | MMR+CT 44; MMR+AT 47; MMR 41 | 84 | Investigate the long-term effects (1 year follow-up) of 12 weeks cognitive (CT) or aerobic (AT) training on cognitive function, psychological health, and work ability for individuals diagnosed with ED. |
| Millet ⁴⁹ | 2008 | Pretest-posttest, pilot | 32 | 100 | To examine whether gardening therapy could be a possible method to be used in the vocational rehabilitation of persons sick-listed due to high levels of stress. |
| Nordh ⁵⁰ | 2009 [†] | Mixed method | 24 | 50 | If individuals with ED on long-term sick-leave can gain improved health when undertaking meaningful activities in a forest (forest-therapy). |
| Olsson ⁵¹ | 2009 | RCT | R. Rosea 30; Placebo 30 | 90 | To determine whether the daily intake of R. rosea extract SHR-5 over a 28-day period would produce any positive effects on attention, quality of life, and symptoms of fatigue and depression in subjects with stress-related fatigue. |

Lindsäter et al 2022; Exhaustion Disorder: Scoping Review of Research

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| Ristiniemi ⁵² | 2014 | Pretest-posttest, case control | African dance 15; ED control 15; Healthy controls 14 | 82 | To systematically study the role of disturbed breathing in individuals with ED and to explore the efficacy of utilizing the African dance of Grounding as a type of short-term physical therapy for normalizing their respiratory patterns. |
| Salomonsson ¹²⁶ | 2017 [†] | RCT | CBT 64; RTW-I 67; COMBO 80 | 82 | To evaluate CBT, a return-to-work intervention (RTW-I) and combined CBT and RTW-I (COMBO) for primary care patients on sick leave due to common mental disorders. |
| Salomonsson ¹²⁷ | 2020 [†] | RCT, subgroup analysis | Stress 152; Control 59 | 82 | To evaluate the effect of CBT for stress-related disorders (adjustment disorder or ED) and explore whether RTW-I, alone or in combination with disorder specific CBT, has different effects for individuals diagnosed with stress-related disorders than for individuals with other primary common mental disorders (depression, anxiety, insomnia). |
| Santoft ¹²⁸ | 2019 | RCT, secondary analysis | CBT 40; RTW-I 42 | 84 | To investigate potential mediators of change for individuals with ED receiving CBT, compared to a return-to-work intervention (RTW-I). |
| Sonntag-Öström ¹²⁹ | 2011 | Mixed method, pilot | 6 | 50 | To examine whether the boreal forest in northern Sweden can be used for rehabilitation from stress-related exhaustion. |
| Sonntag-Öström ⁵⁴ | 2015 | RCT | Forest 51; Control 48 | 86 | To evaluate if participation in the forest intervention can enhance recovery from ED in comparison with the wait-list control group. |
| Sonntag-Öström ¹³⁰ | 2015 | Qualitative | 19 | 84 | Investigate the personal experiences and perceived effects from visits to forest environments in a subset of individuals with severe ED. |
| Stenlund ⁵⁵ | 2009 | RCT | Qigong 41; Control 41 | 83 | Evaluate the effectiveness of "basic care" + a biweekly 12-week Qigong intervention in comparison with only basic care (control condition) in individuals with ED. |
| Strömbäck ¹³¹ | 2020 | Qualitative | 15 | 87 | Investigate experiences from a patient perspective of a dialogue-based workplace intervention with convergence dialogue meetings that was performed by a rehabilitation coordinator. |
| van de Leur ¹³² | 2020 | Longitudinal, cohort | 390 | 88 | Explore changes in ED symptoms and return-to-work-rates in individuals with ED participating in a standardized MMR in a clinical setting. |

[†]Recruitment of blended samples of which ED was a subsample

[‡]Same RCT reporting on different comparison groups and outcomes

Table S5. Overview of dissertations ($N = 17$) for doctoral degree that entail studies on exhaustion disorder.

| Author, year | Study location | Title of thesis | Aim |
|-------------------|--------------------|---|--|
| Engebretsen, 2020 | Oslo, Norway | From dedicated to burned out - and back? A phenomenological exploration of the lived experience of suffering from burnout and implications for medical care | To explore the lived experience of burnout with special attention to the factors they experience as enhancing or restricting their rehabilitation process. |
| Eriksson, 2016 | Sundsvall, Sweden | (In Swedish [†]) At the point of exhaustion. Clinical burn-out as an existential state. Health care providers' and patients' experiences of clinical burn-out and rehabilitation with an existential approach in the Swedish health care context. | To gain insight into the existential experience of clinical burn-out as well as to highlight the significance of an existential perspective in rehabilitation. |
| Finnes, 2018 | Stockholm, Sweden | Return to work - methods for promoting health and productivity in employees on sickness absence | To evaluate the effect of psychological interventions on sickness absence and return to work. |
| Glise, 2014 | Gothenburg, Sweden | Exhaustion disorder - identification, characterization, and course of illness | To study exhaustion disorder (ED) with respect to identification, characterization, and course of illness. Additionally, to study properties of an instrument of self-rated ED (s-ED). |
| Grensman, 2020 | Stockholm, Sweden | Traditional yoga and clinical burnout - quality of life and biomarkers before and after treatment | To understand the situation of patients with clinical burnout (CB) on sick leave, to investigate the effect of traditional yoga (TY) on CB, and whether there are subjective and objective measures that can be used for screening to diagnose CB, to follow the course, and evaluate treatment effects. |
| Gustafsson, 2009 | Umeå, Sweden | (In Swedish [†]) To become or not to become burned out - a complex phenomenon among healthcare professionals in the same workplaces* | To describe the meaning of becoming burnt out and describe personality traits and views on conscience, stress, moral and social support among ED and non-ED participants. |
| Lindsäter, 2020 | Stockholm, Sweden | Cognitive behavioral therapy for stress-related disorders | To build and expand on the limited knowledge base regarding CBT as a treatment for stress-related disorders by further investigating clinical efficacy, cost-effectiveness, and mediators of change in treatment. |

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| Malmberg Gavelin, 2019 | Umeå, Sweden | Rehabilitation for improved cognition in stress-related exhaustion - cognitive neural and clinical perspectives | To evaluate the efficacy of additional cognitive and aerobic training for patients with ED who participated in a multimodal stress rehabilitation program and to explore the neural correlates of ED. |
| Norlund, 2011 | Umeå, Sweden | Psychosocial work factors and burnout - a study of a working general population and patients at a stress rehabilitation clinic | To assess the level of burnout in a working general population and investigate the importance of psychosocial work factors and sex on burnout and to study reduction of sick leave and experiences of returning to work in burnout patients, with special attention towards psychosocial work factors. |
| Persson Asplund, 2021 | Linköping, Sweden | Learning how to recover from stress-related disorders via internet-based interventions | To bring further evidence to the field on the experiences and efficacy of internet-based and work-focused interventions for employees with stress-related disorders. |
| Sahlin, 2014 | Alnarp, Sweden | To stress the importance of nature - nature-based therapy for the rehabilitation and prevention of stress-related disorders | To explore whether Nature-Based Therapy (NBT) for prevention and rehabilitation positively affected participants' health and well-being; that is, their physical and mental health and well-being, as well as their ability to function in everyday life. |
| Salomonsson, 2018 | Stockholm, Sweden | CBT in primary care - effects on symptoms and sick leave, implementation of stepped care and predictors of outcome | To implement and evaluate evidence-based CBT, to evaluate CBT for adjustment and exhaustion disorders, and to evaluate an intervention to reduce sick leave (RTW-I) among patients with common mental disorders in primary care. |
| Santoft, 2019 | Stockholm, Sweden | What makes cognitive behavior therapy work? An investigation of psychological and inflammatory processes | To investigate processes and correlates of therapeutic change in CBT for common mental disorders. |
| Sonntag-Öström, 2014 | Umeå, Sweden | Forest for rest - recovery from exhaustion disorder | To study whether visits to different kinds of forest environments have positive health effects on patients suffering from ED and can be utilized for rehabilitation. |
| Stenlund, 2009 | Umeå, Sweden | Rehabilitation for patients with burnout | To describe patients on long-term sick leave because of burnout and to evaluate rehabilitation programs for this patient group. |

Lindsäter et al 2022; Exhaustion Disorder: Scoping Review of Research

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| Söderström, 2012 | Stockholm, Sweden | Burnout - a matter of impaired recovery? | To investigate physiological and subjective markers of recovery from stress to identify and discuss possible risk factors precipitating burnout, as well as factors related to recovery from burnout and return to work. Sleep and unwinding during leisure time were in particular focus. |
| Wahlberg, 2012 | Stockholm, Sweden | Stress reactivity, cognitive functioning and hippocampal morphology in exhaustion disorder, and development of a self-rating scale for exhaustion disorder, KEDS | To obtain insights into the biological process associated with work stress related depression and exhaustion disorder in women, and to construct and evaluate a self-rating scale for assessment of symptoms of exhaustion disorder. |

[†]Translation to English by research team

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